

METHODS AND APPARATUS FOR NON-INVASIVELY TREATING PATENT
FORAMEN OVALE USING HIGH INTENSITY FOCUSED ULTRASOUND

Reference to Related Applications

[0001] This application claims priority from and is a Continuation-In-Part of United States provisional patent application Serial No. 60/477,532, filed June 10, 2003.

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Field of the Invention

[0002] The present invention relates to methods and apparatus for treatment of patent foramen ovale, and more particularly, to the use of high intensity focused
10 ultrasound non-invasively to treat patent foramen ovale.

Background of the Invention

[0003] Up until the 1980s, there was dramatic growth in the creation of new surgical methods for treating a
15 wide variety of previously untreated conditions. Over the past twenty years there has been a clear trend towards the invention of devices and methods that enable less-invasive treatment of such diseases, moving from invasive surgery, and then to less-invasive surgery, and
20 to interventional techniques. Ultimately, it is desirable to move to totally non-invasive therapies.

[0004] Patent foramen ovale (PFO) is characterized by a persistent fetal opening between the left and right atria of the heart that allows blood to bypass the lungs. In most people, this opening permanently closes during the first few months after birth. However, a PFO is present in up to 15 percent of adults.

[0005] PFO may be associated with various heart conditions including paradoxical embolus, in which an embolus arising in venous circulation gains access to the arterial circulation through the PFO, thereby resulting in stroke or transient ischemic attack. Closure of PFO using a transcatheter approach may be medically necessary for patients with a history of cryptogenic stroke that are not candidates for anticoagulant therapy.

[0006] Implantable devices, such as those of AGA Medical Corporation (Golden Valley, Minnesota) and NMT Medical, Inc. (Boston, Massachusetts) are used to close PFOs.

[0007] It would be desirable to develop methods of treating PFO that are even less invasive than transvascular interventional techniques, thereby eliminating the need for catheters.

[0008] The following devices pertain to the use of high intensity focused ultrasound (HIFU) energy to weld the tissues of a PFO closed. Each device is used for application of energy to the tissues to be sealed. Heating of the tissues of the PFO by the HIFU causes a healing response which causes the formerly separate tissues of the PFO to heal together. In some embodiments, the energy denatures the collagen of the tissues of the different portions of the PFO, and the tissues are caused to remain in close apposition in order to allow the collagen to bond while the tissue return to normal body temperature.

[0008] By way of example, WO 99/18871 and 99/18870 to Laufer, et al. (now abandoned) describe the heating of the tissue of a PFO to induce closure through natural wound healing. These, however are invasive devices which
5 require entering and crossing the PFO. Additionally, U.S. Patent No. 6,562,037 to Paton et al. describes in detail methods and considerations for the rejoining of two tissue sections through the precise application of energy in a two-stage algorithm, wherein all voltage
10 levels used are empirically derived and pre-programmed into the energy delivery control system. Again, however, all devices described would need to be in contact with the tissues to be joined. Relevant articles from the clinical literature include "High-burst-strength,
15 feedback-controlled bipolar vessel sealing", Kennedy et al., Surg Endosc (1998) 12:876-878. This article describes the development of a system for use in open or laparoscopic surgical procedures for achieving hemostasis in large-diameter arteries through the use of RF welding.

20 [0009] A wide variety of energy modes have been used to create lesions using epicardial or intracardiac probes. Radio-frequency electrical energy, microwaves, cryothermia probes, alcohol injection, laser light, and ultrasound energy are just a few of the technologies that
25 have been pursued.

[0010] Separately, several groups have developed focused ultrasound devices with both imaging and therapeutic capabilities. These efforts began perhaps with lithotripsy, in which a high power focused
30 ultrasound system developed by Dornier Medizintechnik, Germany, was used to break up kidney stones in the body. The kidney stones generally are located within the body at a significant depth from the skin. One ultrasound imaging system is used to aim the system at the kidney

stones, and then a second, high energy ultrasound system delivers energy that breaks up the stones so they can be passed.

[0011] More recently, Therus Corp of Seattle, WA, has
5 developed a system to seal blood vessels after the
vessels have been punctured to insert sheaths and
catheters. The Therus system shrinks and seals femoral
artery punctures at a depth of approximately 5 cm.

[0012] In addition, Timi-3 Systems, Inc., Santa Clara,
10 CA, has developed and is testing a trans-thoracic
ultrasound energy delivery system to accelerate the
thrombolysis process for patients suffering an acute
myocardial infarction. This system delivers energy at a
frequency intended to accelerate thrombolysis without
15 damaging the myocardium or vasculature of the heart.

[0013] Epicor Medical, Inc. of Sunnyvale, CA, has
developed a localized high intensity focused ultrasound
("HIFU") device to create lesions in the atrial walls.
The Epicor device is a hand-held intraoperative surgical
20 device, and is configured to be held directly against the
epicardium or outside wall of the heart. When energized,
the device creates full-thickness lesions through the
atrial wall of the heart, and has demonstrated that
ultrasound energy may be safely and effectively used to
25 create atrial lesions, despite presence of blood flow
past the interior wall of the atrium.

[0014] In addition, Transurgical, Inc., Setauket, NY
has been actively developing HIFU devices. However,
while the Epicor Medical devices are placed in close
30 approximation against the outside of the heart, the
Transurgical devices are directed to intravascular
catheters for heating or ablating tissue in the heart and
require that the catheter be brought into close
approximation with the targeted tissue.

[0015] In view of the aforementioned limitations or previously-known devices and methods, it would be desirable to provide methods and apparatus for treating PFO by heating or ablating tissue at a distance from that tissue, so that the procedure may be performed non-invasively.

[0016] It also would be desirable to provide methods and apparatus for treating PFO by applying energy from outside the body or from organs, such as the esophagus, that are easily accessible via natural body openings.

Summary of the Invention

[0017] In view of the foregoing, it is an object of the present invention to provide methods and apparatus for treating PFO so as to cause closure by ablating or applying energy to weld the tissue at a distance from that tissue, so that the procedure may be performed non-invasively.

[0018] It is another object of the present invention to provide methods and apparatus for treating PFO by applying energy from outside the body or from neighboring organs, such as the esophagus, that are easily accessible.

[0019] These and other objects of the present invention are accomplished by providing methods and apparatus that enable a physician to image tissue within the body that is to be heated or ablated, and then to heat or ablate that tissue using a completely or relatively non-invasive procedure, and with little or no anesthesia. Advantageously, the methods and apparatus of the present invention are expected to be cost-effective and time-efficient to perform compared to the previously-known surgical and interventional procedures.

Brief Description of the Drawings

[0020] The above and other objects and advantages of the present invention will be apparent upon consideration of the following detailed description, taken in

5 conjunction with the accompanying drawings, in which like reference characters refer to like parts throughout, and in which:

[0021] FIG. 1 is a schematic view of an illustrative imaging and treatment ultrasound system of the present
10 invention;

[0022] FIG. 2 is a schematic view of an illustrative display of the imaging and treatment ultrasound system of the present invention;

[0023] FIG. 3 is a schematic view showing the imaging and treatment ultrasound system of FIG. 1 disposed
15 adjacent to a cross-section of a patient's thorax; and

[0024] FIG. 4 is a schematic view of the distal region of a catheter-based high intensity focused ultrasound array.

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Detailed Description of the Invention

[0025] The present invention is directed to methods and apparatus for creating lesions in the walls of the heart or for ablating or welding the tissue of a PFO in a

25 non-invasive manner using high intensity focused ultrasound (HIFU). Previously-known HIFU systems, such as those being developed by Epicor Medical or Transurgical, require close approximation of the HIFU device to the target tissue. These systems are not
30 adapted for PFO closure. The methods and apparatus of the present invention overcome this drawback by providing systems that enable the creation of lesions in the heart wall from a greater distance.

[0026] Referring to FIG. 1, apparatus constructed in accordance with the principles of the present invention is described. System 10 comprises head 11 housing ultrasound imaging system 12 and high intensity focused
5 ultrasound energy ("HIFU") system 14. Ultrasound imaging system 12 and HIFU system 14 may have in common all or just a subset of the transducers and related components, operating in different modes to image or ablate. Head 11 is mounted on arm 13 that permits the head to be
10 positioned in contact with a patient (not shown) lying on table 15. Head 11 also may be a handheld unit, not needing an arm 13 to support or position it. System 10 includes controller 16 that controls operation of imaging system 12 and HIFU system 14. Monitor 18 displays images
15 output by imaging system 12 that allows the clinician to identify the desired locations on the walls of the heart to be treated.

[0027] In accordance with the methods of the present invention, controller 16 and monitor 18 also are
20 programmed to indicate the focus of the HIFU energy relative to the image of the tissue cross-section. FIG. 2 shows illustrative screen display 19 of monitor 18 wherein the outline **T** of the tissue, as imaged by imaging system 12, and a marker corresponding to the location of
25 focal point **F** of HIFU system 14, may be seen.

[0028] When activated, the HIFU system delivers ablative energy to the specific location shown on monitor 18 (focal point **F** in FIG. 2), thus enabling safe creation of lesions or tissue welds. Because the HIFU system is
30 configured to deliver energy from a number of sources focused towards the target tissue area, intervening tissue is subjected to only a fraction of the energy deposited in the target tissue receives, and thus the

intervening tissue is not significantly heated or ablated.

[0029] Referring still to FIG. 1, ultrasound imaging system 12 may be similar in design to previously-known trans-thoracic ultrasound imaging systems, and are per se known. High intensity focused ultrasound system 14 may comprise one or more HIFU generators 20 constructed as described in U.S. Patent Publication No. US20010031922A1. As mentioned before, imaging system 12 and HIFU system 14 also may use common elements. Preferably, each HIFU generator 20 is the same as or is disposed approximately in the same plane as the imaging elements of ultrasound imaging system 12, so that the focus of HIFU system 14 occurs in the plane of the target tissue imaged by ultrasound imaging system 12. In addition, this arrangement advantageously ensures that the HIFU energy will reach the target.

[0030] In a preferred embodiment, HIFU generators 20 deliver energy at a frequency optimized for heating myocardium, so that the lesions created will weld, occlude, or lead to the occlusion of the patent foramen ovale. Once the lesions are created, a gradual healing process is begun in which the lesions fibrose, thus permanently sealing the opening.

[0031] While it may be possible to image and heat simultaneously, it may occur that the output of HIFU system 14 may interfere with the ability to image the tissue using ultrasound imaging system 12. Accordingly, controller 16 may be programmed to time-gate operation of imaging system 12 and HIFU system 14, so that the tissue is alternately imaged and ablated at a frequency of up to several times per second.

[0032] In order to apply energy to the wall of the septa of the heart sufficient to occlude the PFO, it may

be desirable to slowly move the focus of the HIFU system along the wall of the septa during the ablation process. While this may be accomplished by manually moving the HIFU system, it may alternatively be desirable to
5 automate the process. For example, controller 16 may include suitable programming and joystick 22, or other input device, for refocusing the focal point of HIFU system 14 along a desired trajectory.

[0033] Referring now to FIG. 3, according to an aspect
10 of the present invention, an exemplary method of using the HIFU system to treat PFO is described. More particularly, the HIFU system is used to create localized tissue heating of the septum primum and septum secundum that will lead to occlusion of a PFO. The consequent
15 healing process is expected to cause the septum primum and septum secundum to heal together, thereby permanently closing the PFO or resulting in acute welding of the tissues. Even if this non-invasive treatment were to be effective in closing PFO in only a small percentage of
20 cases, the procedure would likely become the first choice for use in initial therapy.

[0034] The tissues of the septum primum and the septum secundum preferably are in contact when the energy is applied to facilitate welding of the PFO. In cases where
25 heat is applied to cause closure through scar formation and subsequent healing, it is also desirable to have the tissue in apposition to ensure that the correct target tissues are heated to an adequate degree to cause tissue damage. Adequate apposition exists in many patients in
30 the absence of an elevated right atrial pressure. However, in some cases it may be necessary or desirable to artificially increase the pressure gradient between the right and left atria to ensure closure of the PFO

and/or to increase the contact pressure between the septum primum and septum secundum.

[0035] Closure of the PFO or increased contact pressure between the septum primum and septum secundum
5 can be achieved noninvasively through a variety of known techniques using medications, mechanical expedients, or a combination of the two. By way of example, briefly applying external pressure to a patient's jugular veins will temporarily limit blood flow into the superior vena
10 cava and hence the right atrium. Of course, this lowers the right atrial pressure relative to the left atrial pressure, thereby creating the desired closure or increase in contact pressure. Alternatively, the desired closure or increase in contact pressure may be achieved
15 by administering drugs that increase the patient's blood pressure by increasing heart rate and/or peripheral resistance. One suitable drug for increasing heart rate is epinephrine. As a further alternative, such drugs may be administered in combination with the application of
20 pressure to the patient's jugular veins.

[0036] In the system shown in FIG. 3 the focus of the HIFU system is fixed at a certain point within the field of the ultrasound image. For example, the ultrasound image might show a picture of rectangular planar cross-
25 section of tissue with a fixed focus of the HIFU energy in the center of the field. In operation, the clinician manually moves the probe until the desired tissue is in the target area, and then fires the HIFU system to ablate the tissue and occlude or weld the PFO. In order to
30 ablate tissue located less than 130 mm below the skin and still retain a continuous fluid path from the probe to the target, the HIFU system includes fluid-filled balloon
24 that covers the face of the probe.

[0037] Balloon 24 preferably is filled with water and enables the clinician to reposition the probe at a variable distance from the skin. Balloon 24 also permits the clinician to position the probe at any desired angle to target tissue not aligned directly under the focal point of HIFU system 14. Alternatively, the patient could sit in a tub of water, so the patient's chest and the probe were both underwater, again ensuring a continuous fluid path.

10 [0038] As a further alternative, controller 16 may be programmed so that the depth of the focal point of the HIFU system is depth-adjustable relative to the imaged tissue. Advantageously, the depth of the targeted tissue then could be adjusted relative to the imaged field, so a smaller fluid-filled balloon, or no balloon, is used to maintain fluid contact while adjusting the angle of the imaged section or make minor changes in the depth of the targeted tissue. WIPO Patent Publication No. WO/0145550A2 to Therus describes several ways to adjust the depth of the focused energy by changing the radius of curvature of one or more of the ultrasound generators. Alternatively, the direction of several focused energy generators of relatively fixed focal length could be shifted relative to one another to move the focal point.

25 [0039] In accordance with the principles of the present invention, focused energy is applied from outside the patient's body. Because ultrasound energy does not travel coherently through non-fluid filled tissue, such as the lungs, positioning of the ultrasound imaging system and HIFU system at certain angles may be more advantageous for treatment of specific areas of the heart.

[0040] Accordingly, it may be desirable to locate the imaging system and HIFU system on a movable arm or to

position it by hand so as to permit other external approaches, such as from below the diaphragm on the left anterior side of the body, so the ultrasound has a coherent path through the diaphragm and apex and
5 ventricles of the heart to the septa. Application of the probe also may be made along a patient's back.

[0041] While in the preferred embodiment described hereinabove energy is delivered from outside the body, situations may arise where it is difficult to deliver the
10 energy to the PFO tissue. Referring now to FIG. 4, and in accordance with another aspect of the present invention, methods and apparatus are provided for positioning a probe inside the body and closer to the targeted tissue, but still not necessarily adjacent to
15 it. Intraluminal probe 30 is configured to deliver HIFU energy to the heart from the esophagus, from the aorta, or from the great veins of the heart such as the inferior vena cava, superior vena cava, or the right atrium itself.

20 [0042] This approach is fundamentally different from previously-known methods of performing ablation during surgical procedures using epicardial probes or during interventional procedures using intracardiac ablation catheters. These previously-known devices are designed
25 to be in direct contact or at least very close proximity (e.g., within 5 mm) of the target tissue, and are not designed to avoid ablation of intervening tissue between the probe and the target tissue.

[0043] Still referring to FIG. 4, catheter 30
30 preferably has a diameter in a range of 5 to 10 mm for vascular devices, and a diameter in a range of 5 to 20 mm for an esophageal device. Imaging elements 32 and HIFU elements 34 are arranged linearly along the longitudinal axis of the catheter.

[0044] The linear nature of the imaging element and HIFU element array may impose limitations on the ability to reposition the device. While translation and rotation of the catheter may be relatively easy, it is
5 contemplated that it may be difficult to move the device very far to one side or another within a relatively small-diameter body lumen.

[0045] Accordingly, intraluminal catheter 30 preferably is configured to adjust the focal point of the
10 HIFU system with respect to both longitudinal position and depth. This may be accomplished by programming the controller used with intraluminal catheter 30 to adjust the focal point of the HIFU system, as described above. Alternatively, refocusing of the array of HIFU elements
15 may be achieved by locating individual HIFU elements on independently steerable actuators 36. Actuators 36 are controlled by the system controller and permit the clinician to move the focal point of the HIFU array to any desired point in the field of view of the imaging
20 system.

[0046] In accordance with another aspect of the present invention, methods of using intraluminal catheter 30 to heat or ablate septal tissues from the esophagus to treat PFO are described. The esophagus is separated from
25 the PFO by only about 20 - 25 mm, such that a lesion may be easily made in the PFO using a probe capable of delivering energy at a distance of approximately 20 - 50 mm.

[0047] As described above, intraluminal catheter 30
30 preferably is configured, either mechanically or by suitable software algorithms, to move its focal point to enable a continuous linear ablation or heat affected zone without moving the device. Alternatively, the HIFU array of the catheter may be configured to create a linear

ablation or heat affected zone, or have a fixed-focus so that a linear ablation or heat affected zone may be created by translating the HIFU array within the esophagus.

5 **[0048]** In addition, it may be beneficial to cool tissue surrounding the HIFU array of intraluminal catheter 30, to further reduce the risk of damage to the esophagus. Intraluminal catheter 30 may therefore include a water jacket that circulates fluid around the
10 HIFU array to prevent any heat generated by the array or ultrasound energy absorbed by the esophagus from causing any tissue damage.

[0049] Although preferred illustrative embodiments of the present invention are described above, it will be
15 evident to one skilled in the art that various changes and modifications may be made without departing from the invention. It is intended in the appended claims to cover all such changes and modifications that fall within the true spirit and scope of the invention.